

Amendments to the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

1. (withdrawn) Human polypeptide designated Cyk-4, which is a GTPase activating protein (GAP) for Rho family of GTPases, with the amino acid sequence as set forth in SEQ ID NO:2 or with the amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

2. (withdrawn) Murine Cyk-4 polypeptide designated Cyk-4, which is a GTPase activating protein (GAP) for Rho family of GTPases, with the amino acid sequence as set forth in SEQ ID NO:4 or with the amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

3. (withdrawn) An isolated DNA molecule comprising a polynucleotide with the nucleotide sequence as set forth in SEQ ID NO:1 encoding human Cyk-4 polypeptide, or an isolated DNA molecule encoding human Cyk-4 polypeptide comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

4. (withdrawn) An isolated DNA molecule comprising a polynucleotide with the nucleotide sequence as set forth in SEQ ID NO:3 encoding murine Cyk-4 polypeptide, or an isolated DNA molecule encoding murine Cyk-4 polypeptide comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

5. (withdrawn) An antibody which is specifically reactive with an epitope of the human Cyk-4 polypeptide of claim 1.

6. (withdrawn) An antibody which is specifically reactive with an epitope of the murine Cyk-4 polypeptide of claim 2.

7-11. (cancelled)

12. (withdrawn) A compound identified in the method of any one of claims 7 to 11 for use in cancer therapy.

13-44. (cancelled)

45. (currently amended) A method for ~~identifying a compound having~~ determining whether a compound has the potential to inhibit cytokinesis by determining the compound's ability to inhibit the function of a CYK-4 protein or fragment of the CYK-4

protein fragment thereof to promote GTP hydrolysis by a Rho family GTPase, the method comprising:

- (i) incubating the Rho family GTPase with GTP for a period of time sufficient to allow saturation of the Rho family GTPase's GTP binding sites;
- (ii) adding the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ to the Rho family GTPase and the GTP in the presence and absence of ~~a test~~ the compound, wherein the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ comprises a GTPase activating protein domain; and
- (iii) determining an amount of GTP that is hydrolyzed in the presence and absence of the ~~test~~ compound;

wherein the ~~test~~ compound is ~~identified as a compound having~~ determined to have the potential to inhibit cytokinesis if the ~~test~~ compound inhibits the CYK-4 stimulated GTP hydrolysis determined in (iii); and

wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

46. (previously presented) The method of claim 45, wherein the Rho family GTPase is a full-length Rho family GTPase protein or a fragment of the Rho family GTPase protein that retains GTPase activity.

47. (cancelled)

48. (currently amended) The method of claim 46 ~~claim 47~~, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

49. (previously presented) The method of claim 48, wherein the Rho family GTPase is selected from the group consisting of human RhoA, human RhoB, human RhoC, human RAC1, human RAC2, human RAC3, and human GB25.

50. (previously presented) The method of claim 49, wherein the Rho family GTPase is human RhoA.

51. (previously presented) The method of claim 46, wherein the Rho family GTPase is immobilized on a solid support.

52. (previously presented) The method of claim 46, wherein the GTP is labeled.

53. (previously presented) The method of claim 52, wherein the GTP is labeled with a radioisotope or a fluorescent label.

54. (currently amended). A method for ~~identifying a compound having~~ determining whether a compound has the potential to inhibit cytokinesis by determining the compound's ability to inhibit ~~interfere with~~ the function of a CYK-4 protein or fragment of the CYK-4 protein ~~a fragment thereof~~ to bind to ~~members~~ a member of the MKLP1 subfamily of kinesin-like proteins, the method comprising:

(i) incubating a the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ for a period of time with ~~an~~ the MKLP1 protein subfamily member, in the presence and absence of ~~a test~~ the compound, wherein the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ comprises a domain that binds MKLP1 subfamily proteins; and

(ii) determining an amount of the MKLP1 protein subfamily member bound to the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ in the presence and absence of the ~~test~~ compound;

wherein the ~~test~~ compound is ~~identified as a compound having~~ determined to have the potential to inhibit cytokinesis if the ~~test~~ compound inhibits ~~interferes with~~ the binding of the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ to the MKLP1 protein subfamily member as determined in (ii); and

wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide

which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

55. (currently amended) The method of claim 54, wherein the MKLP1 protein subfamily member is a full-length MKLP1 protein or a fragment of the MKLP1 protein subfamily member that comprises a domain that binds the CYK-4 protein or fragment of the CYK-4 protein.

56. (currently amended) The method of claim 55, wherein the MKLP 1 protein subfamily member is selected from the group consisting of CeM03D4.1b (~~C. elegans~~; ~~GenBank ID U61955, Protein ID 1397342~~) (SEQ ID NO:7) and HsMKLP1 (~~human~~; ~~GenBank ID X67155; SwissProt Q02241~~) (SEQ ID NO:8).

57. (currently amended) The method of claim 56, wherein the MKLP 1 protein subfamily member is HsMKLP1 (SEQ ID NO:8).

58. (cancelled)

59. (currently amended) The method of claim 56 ~~claim 58~~, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a

protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

60. (currently amended) The method of claim 59 ~~claim 58~~, wherein the fragment of the CYK-4 protein comprises amino acid residues 1-120 of human CYK-4 (SEQ ID NO:2).

61. (currently amended) The method of claim 55, wherein the CYK-4 protein or fragment of the CYK-4 protein ~~fragment thereof~~ is immobilized on a solid support, and wherein the MKLP1 protein subfamily member or fragment of the MKLP1 protein subfamily member ~~fragment thereof~~ is labeled.

62. (previously presented) The method of claim 61, wherein the label is a radioisotope, a fluorescent label, or a hapten.

63. (previously presented) The method of claim 55, wherein step (i) is performed in solution.

64. (currently amended) A method for ~~identifying a compound having~~ determining whether a compound has the potential to inhibit cytokinesis by determining the compound's ability to inhibit CYK-4 function by determining the compound's ability to

inhibit self association of a CYK-4 protein or fragment of the CYK-4 protein ~~a fragment thereof~~, the method comprising:

(i) incubating in the presence and absence of ~~a test~~ the compound a first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ with a second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~, wherein the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ and the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ each comprises a domain that mediates CYK-4 protein self-association, and wherein the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ is labeled; and

(ii) determining an amount of the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ bound to the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~;

wherein the ~~test~~ compound is ~~identified as a compound having~~ determined to have the potential to inhibit cytokinesis if the ~~test~~ compound inhibits the binding of the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ to the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ as determined in (ii); and

wherein the first CYK-4 protein and the second CYK-4 protein are each selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a

polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

65-66. (cancelled)

67. (currently amended) The method of claim 64 ~~claim 66~~, wherein the first CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

68. (currently amended) The method of claim 67 ~~claim 65~~, wherein the fragment of the first CYK-4 protein comprises amino acid residues 1-120 of human CYK-4 (SEQ ID NO:2).

69. (currently amended) The method of claim 68 ~~claim 66~~, wherein the fragment of the second CYK-4 protein comprises amino acid residues 1-120 of human CYK-4 (SEQ ID NO:2).

70. (currently amended) The method of claim 64, wherein the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ is immobilized on a solid support, and wherein the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ is labeled.

71. (currently amended) The method of claim 70, wherein the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~ is labeled with a radioisotope label, a fluorescent label, a hapten label, a peptide label, or an enzyme label.

72. (currently amended) The method of claim 64, wherein the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ is identical to the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~.

73. (currently amended) The method of claim 64, wherein the first CYK-4 protein or fragment of the first CYK-4 protein ~~fragment thereof~~ is different from the second CYK-4 protein or fragment of the second CYK-4 protein ~~fragment thereof~~.

74. (withdrawn) A method for identifying a compound having the potential to inhibit cytokinesis by determining the compound's ability to inhibit CYK-4 function by determining the compound's ability to inhibit self association of a member of the MKLP1 subfamily of kinesin-like proteins or a fragment thereof, the method comprising:

(i) incubating in the presence and absence of a test compound a first MKLP1 protein subfamily member or fragment thereof with a second MKLP1 protein subfamily member or fragment thereof, wherein the first MKLP1 protein subfamily member or fragment thereof and the second MKLP1 protein subfamily member or fragment thereof each comprises a domain that mediates self-association of MKLP1 subfamily proteins,

and wherein the second MKLP1 protein subfamily member or fragment thereof is labeled; and

(ii) determining an amount of the second MKLP1 protein subfamily member or fragment thereof bound to the first MKLP1 protein subfamily member or fragment thereof;

wherein the test compound is identified as a compound having the potential to inhibit cytokinesis if the test compound inhibits the binding of the first MKLP1 protein subfamily member or fragment thereof to the second MKLP1 protein subfamily member or fragment thereof as determined in (ii).

75. (withdrawn) The method of claim 74, wherein the first MKLP1 protein subfamily member or fragment thereof is immobilized on a solid support.

76. (withdrawn) The method of claim 74, wherein the second MKLP1 protein subfamily member or fragment thereof is labeled with a radioisotope label, a fluorescent label, a hapten label, a peptide label, or an enzyme label.

77. (withdrawn) The method of claim 74, wherein the first MKLP1 protein subfamily member or fragment thereof is identical to the second MKLP1 protein subfamily member or fragment thereof.